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(54) Detecting mis-use of drugs

(57) A composition comprising an administrable drug, such as methadone and a marker that can be detected visually in a urine sample taken from a recipient of the composition. A suitable marker is methylene blue or phenolphthalein. Also disclosed is composition comprising an administrable drug and a substance capable of inducing a harmless but unpleasant effect on the recipient when the drug is taken intravenously instead of orally.

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TITLE: Administration of drugs.

DESCRIPTION

This invention concerns administration of drugs.

Methadone is commonly used in aqueous solution for oral administration to heroin addicts to reduce the severity of drug withdrawal symptoms. Methadone mixture is a standard formulation, sweetened either with sucrose or artificial sweetening agents, both being coloured green in compliance with the Drug Tariff formulation. The colourants used either are not absorbed in the gut or are metabolised.

Unfortunately the prescription of methadone in this way is open to abuse because methadone has a "street value". Thus, the methadone solution prescribed can be further diluted by a patient and amounts thereof sold on. Of course, money obtained in this way may regrettably be used by the patient to buy more heroin.

Because of the possible abuses of methadone, it would be helpful to have a simple way of determining either whether a patient has taken their prescribed dose of methadone or, indeed, if some other person has taken a dose not prescribed to them. Tests can be carried out for such determination but require taking of body samples for analysis in a laboratory. Obviously, that can be time consuming and costly. Similar problems can arise with other prescribed drugs.

An object of this invention, therefore, is to provide a relatively simple way of determining whether a person has taken a particular drug.

According to the present invention there is provided a composition comprising an administrable drug and a marker visually detectable in a sample taken from a person who has taken the drugs composition.

In one preferred embodiment of the invention, the marker is a dye that is unmetabolised at least to the extent that sufficient of the marker passes through the body and is secreted into the urine which is accordingly coloured. A suitable dye for this purpose has been found to be methylene blue.

In another preferred embodiment, the marker is a substance excreted into the urine whose presence is detectable by reaction with a reagent. Typically such a marker will be colourless in the urine but will change colour in the presence of a suitable reagent. A marker that changes colour with a change of pH is preferred for this purpose. A suitable marker in this instance would be phenolphthalein which is partially excreted into the urine. On addition of an alkaline reagent to render a urine sample alkaline, phenolphthalein turns pink. Thus, sodium hydroxide solution could be added to the urine sample. Alternatively suitable papers impregnated with the reagent may be used to test for the presence of the marker.

Such reagent papers may also be subjected to chromatographic treatment for comparison of the result obtained with known standards.

In yet another preferred embodiment the marker is a substance secreted in the urine and which fluoresces under, for example, UV light.

Compositions of the invention may be in the form of liquids for oral administration or in the form of tablets. Compositions of the invention

may be used with any suitable drug where confirmation that it has been taken is desirable or where it is desirable to determine if someone other than the patient has taken the drug. Methadone is one drug that is particularly suitable for compositions of the invention. Methadone is used to bring drug users off heroin but it still has a "street value", so that users of methadone can be tempted to sell their supply rather than use it themselves. By administering methadone in the form of compositions of the invention, such mis-use can be easily detected.

Compositions of the invention may also be suitable for use on patients for whom compliance with drug dosage regimes is critical to their treatment but which cannot readily be tested. For example, the use of powerful antipsychotics by manic depressives and schizophrenics in the community is often difficult to follow and requires samples being taken to a laboratory for analysis, which takes time. Thus, the use of a drug composition containing a marker according to the invention can make useful information speedily available to a care team following a simple test process carried out by a care worker visiting the patient.

For example, lithium tablets used to control mania may be marked in accordance with the invention and a visiting psychiatric social worker can monitor whether or not a patient is complying with their prescribed dosage regime providing a useful interim check in between necessary evaluation of blood lithium levels which are determined at longer intervals.

Drugs used to suppress criminal sexual activities may be suitable for compositions according to the invention, especially as the detection of

compliance with the required dosage regime is relatively non-intrusive. A specific example in this area is the administration of benperidol tablets to offenders after release on such medication and indeed prisoners in possession of their own medication within prison or other institutions.

A problem that occurs with some drugs intended for oral administration is that they are used intravenously. That is a particular problem with methadone solutions. To dissuade patients from intravenous administration of drugs it is further proposed herein that compositions according to the invention include a substance that induces a harmless but unpleasant effect on a patient, such as nausea and/or vomiting, when taken intravenously but not when taken orally. The use of a dye marker which is not absorbed following oral administration but is excreted via the urine, if injected intravenously would indicate an inappropriate route of administration.

The invention further provides a composition comprising an administrable drug and a substance that induces a harmless but unpleasant effect on a patient when the composition is taken intravenously but not when taken orally, such as nausea and/or vomiting.

Preferably compositions of the invention include an emetic substance, such as, for example, apomorphine.

It is envisaged that liquid compositions of the invention will be provided in unit doses that can be identified, whereby a record can be kept of the recipient of a unit dose with the aim of being able to prevent a patient from receiving a second unit dose unless the container of the first unit dose is

returned by the original recipient. In that way it may be possible to limit occurence of such doses of drugs being disposed of by the patient for gain. In one preferred embodiment of the invention such doses will be in containers bearing two part labels, one part of which is adhered to the container and the other part is removable. Both parts of the label will carry the same identification information, the removable, e.g. tear-off part being retained by the issuing pharmacist, so that the container can be traced back to the patient, if necessary. The tear-off part is preferably a self-adhesive patch that can be stuck in to the Controlled Drugs Register at the issuing pharmacy. Other means of marking and recording containers may, of course, be used, such as, for example, bar coding.

It is further preferred that containers for compositions of the invention be supplied in childproof containers. Preferably the containers are double sealed.

This invention will now be further described by means of the following Examples.

Example 1

Methadone hydrochloride solutions were prepared by dissolving in water the following amounts: 1mg/ml, 2mg/ml, 3mg/ml and 5mg/ml. Each solution was flavoured with xylitol in an amount of about 2% w/v.

The different strength solutions were packaged in unit doses for oral consumption in a range of volumes, namely 2.5ml, 5ml, 10ml and 25ml for the 1mg/ml and 2mg/ml strength solutions and 5ml, 10ml and 25 ml for

the 3mg/ml and 5mg/ml strength solutions.

Each unit dose had 10mg of methylene blue dye added. Methylene blue is secreted unmetabolised into urine causing a detectable colour change in the urine.

Example 2

All of the solutions prepared in Example 1 were repeated with phenolphthalein as the dye instead of methylene blue.

Phenolphthalein is partially excreted in urine. It has an acid pH and is colourless in acid but pink in alkaline. Hence, the oral solution and the urine are colourless. By addition of alkali, such as sodium hydroxide, to the urine, urine is rendered alkaline, which reveals the pink colour of phenolphthalein. Alternatively, the urine could be added to a filter paper impregnated with colour change reagent.

Example 3

The solution of Examples 1 and 2 were repeated with the addition of 3mg of apomorphine per unit dose. Apomorphine is a powerful emetic, so that if an oral solution containing it was injected, nausea and vomiting would result. On the other hand, if the oral solution is taken correctly, i.e. by mouth, the apomorphine merely acts as an expectorant, reducing the viscosity of the sputum.

CLAIMS

1. A composition comprising an administrable drug and a marker visually detectable in a sample taken from a person who has taken the composition.

2. A composition as claimed in claim 1, wherein the marker is detectable in a person's urine sample.

3. A composition as claimed in claim 2, wherein the marker is a dye that is unmetabolised at least to the extent that sufficient of the marker passes through the body and is secreted into the urine which is accordingly coloured.

4. A composition as claimed in claim 1, 2 or 3, wherein the marker is methylene blue.

5. A composition as claimed in claim 1, wherein the marker is a substance secreted in the urine whose presence is detected by reaction with a reagent.

6. A composition as claimed in claim 5, wherein the marker is colourless in the urine but changes colour in the presence of a suitable reagent.

7. A composition as claimed in claim 5 or 6, wherein the marker changes colour with a change of pH.

8. A composition as claimed in claim 5, 6 or 7, wherein the marker is phenolphthalein.

9. A composition as claimed in claim 1 or 2, wherein the marker fluoresces.

10. A composition as claimed in claim 9, wherein the marker fluoresces under UV light.

11. A composition as claimed in any one of claims 1 to 10, wherein the

administrable drug is methadone.

12. A composition as claimed in any one of claims 1 to 10, wherein the administrable drug is in the form of lithium tablets for controlling mania.

13. A composition as claimed in any one of claims 1 to 10, wherein the administrable drug is benperidol.

14. A composition as claimed in any one of claims 1 to 13 further comprising a substance capable of inducing a harmless but unpleasant effect on the recipient when the composition is taken intravenously instead of orally.

15. A composition as claimed in claim 14, wherein the unpleasant effect is nausea and/or vomiting.

16. A composition as claimed in claim 14 or 15, wherein the substance capable of inducing a harmless but unpleasant effect is apomorphine.

17. A composition as claimed in any one of claims 1 to 16 in a liquid dosage container having a two part label, one part being removable for retention by an issuing pharmacist and the other remaining on the container, whereby the container can be traced back to the recipient.

18. A composition as claimed in any one of claims 1 to 17 in a childproof container.

19. A composition as claimed in any one of claims 1 to 18, in a double sealed container.

20. A composition comprising an administrable drug and a substance capable of inducing a harmless but unpleasant effect on a recipient when the drug is taken intravenously instead of orally.

21. A composition as claimed in claim 20 or 21, wherein such substance is apomorphine.

23. An administrable drug composition substantially as hereinbefore described with reference to any one of the foregoing Examples.

The Patent Office

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Claims searched:	1-19, (23 in respect of Examples 1 & 2)	**Date of search:**	28 April 1997

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Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.O): A5B

Int Cl (Ed.6): A61K

Other: ONLINE: WPI, Chemical Abstracts

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X	US 4223004	(HSIA) see colum 8 line 63-column 9 line 12 & column 11 line 57- column 12 line 39.	1, 2, 11, 18 at least
A	WO 88/09495 A1	(DRUG SCREENING SYSTEMS)	

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.